60th Medical Group (AMC), Travis AFB, CA

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)

FINAL REPORT SUMMARY

(Please type all information. Use additional pages if necessary.)

PROTOCOL #: FDG20130030A **DATE:** 23 April 2014

PROTOCOL TITLE: Pilot Study: Wound healing with CorMatrix® in the rabbit (*Oryctolagus cuniculus*).

PRINCIPAL INVESTIGATOR (PI) / TRAINING COORDINATOR (TC): Lt Col Antoinette Shinn

DEPARTMENT: 60 MDG/SGSE **PHONE #:** 423-7267

INITIAL APPROVAL DATE: 3 June 2013 **LAST TRIENNIAL REVISION DATE:** N/A

FUNDING SOURCE: SG Office

1. RECORD OF ANIMAL USAGE:

Animal Species:	Total # Approved	# Used this FY	Total # Used to Date
Oryctolagus cuniculus	**10**	**5**	**5**

2. PROTOCOL TYPE / CHARACTERISTICS: (Check all applicable terms in **EACH** column)

___ Training: Live Animal ___ Medical Readiness ___ Prolonged Restraint

___ Training: non-Live Animal ___ Health Promotion ___ Multiple Survival Surgery

_X_ Research: Survival (chronic) ___ Prevention ___ Behavioral Study

___ Research: non-Survival (acute) ___ Utilization Mgt. ___ Adjuvant Use

_X_ Other (Model/Technique Perfecting)___ Other (Treatment) ___ Biohazard

3. PROTOCOL PAIN CATEGORY (USDA): (Check applicable) ___ C _X_ D ___ E

4. PROTOCOL STATUS:

***Request Protocol Closure:**

___ Inactive, protocol never initiated

___ Inactive, protocol initiated but has not/will not be completed

_X Completed, all approved procedures/animal uses have been completed

5. FUNDING STATUS: Funding allocated: $4850.00 Funds remaining: $ 0.00

6. PROTOCOL PERSONNEL CHANGES:

Have there been any personnel/staffing changes (PI/CI/AI/TC/Instructor) since the last IACUC approval of protocol, or annual review? _X_ Yes ___ No

If yes, complete the following sections (Additions/Deletions). For additions, indicate whether or not the IACUC has approved this addition.

ADDITIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, IACUC approval - Yes/No)

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
15 APR 2014	**Final**	**3 Jun 2013 - 15 Apr 2014**

4. TITLE AND SUBTITLE **FDG20130030A "Pilot study: Wound healing with CorMatrix in the rabbit (Oryctolagus cuniculus)."**	5a. CONTRACT NUMBER 5b. GRANT NUMBER 5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S) **Lt Col Antoinette Shinn, J. Kevin Grayson, DVM, Ph.D.**	5d. PROJECT NUMBER **FDG20130030A** 5e. TASK NUMBER 5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) **Clinical Investigation Facility David Grant Medical Center 101 Bodin Circle Travis AFB, CA 94535**	8. PERFORMING ORGANIZATION REPORT NUMBER
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) **Clinical Investigation Facility David Grant Medical Center 101 Bodin Circle Travis AFB, CA 94535**	10. SPONSOR/MONITOR'S ACRONYM(S) 11. SPONSOR/MONITOR'S REPORT NUMBER(S)
12. DISTRIBUTION/AVAILABILITY STATEMENT **Approved for public release, distribution unlimited**	
13. SUPPLEMENTARY NOTES	

14. ABSTRACT

Objective: Technique perfecting for wound healing model in the rabbit Results: Using the five rabbits for technique perfecting proved very beneficial for the investigator. Multiple lessons were learned. 1. The CorMatrix covered the ear wounds best when they were made slightly larger than the wound. Originally, the ear wounds and CorMatrix patches were both cut with a 6mm biopsy punch. This made stitching the patch in place on all sides difficult. The patch was flush with the wound on one side and not necessarily on the opposite side. When the wound was made with a 5mm biopsy punch and the patch with the 6mm punch, the patch easily covered the entire wound on all sides when secured in place. 2. Four wounds per ear was optimum. More than four wound made it difficult (if not impossible) to avoid lacerating a large blood vessel or creating a wound proximal to the ear orifice (an area difficult to place a wound dressing). It also made it difficult to maintain consistent spacing between each wound in an area of the ear that could have a dressing applied. 3. The original spacing between the wounds was 30 mm. That is much larger than necessary or desired. The 30mm distance made applying a dressing to cover all four wounds challenging. Making the wounds 10-15mm apart kept the wounds far enough apart to easily suture the treatment patches in place and not cross contaminate the controls. It also made it much easily to apply a dressing to the ears. 4. Each stitch required a minimum of four throws to tack the CorMatrix in place on four quadrants. The PDS suture has memory and easily unties when not adequately secured. In the first animals, only two throws per stitch were performed and the patches did not remain in place. Upon examination of corresponding histology slides there was no evidence of the CorMatrix patches. When four throws were used to secure the patches, the patch was verified by the histology results. 5. The 5-0 PDS worked much better than 5-0 Vicryl for suturing the patches in place. The Vicryl did not move through the tissue and cartilage smoothly (it was very rough). 6. The Tegaderm dressing worked best when only a small piece was (cut to size) used on the ear. However it would only last one day at best, before coming off the ear. Bacitracin ointment applied twice a day worked well to keep the wound beds moist. However, the bacitracin ointment applied to the wounds with a Vaseline/petroleum gauge place over it appeared to be the best ear dressing (for maintain wound moisture) and would remain in place for at least a day (possibly two days) before changing. 7. EMLA cream could also be applied post operatively before the dressing is applied for postoperative analgesia. 8. The wounds healed very quickly and were completely healed before 28 days post wounding.

15. SUBJECT TERMS

US Air Force, Medical Service, Medical Research, Graduate Medical Education

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
unclassified	**unclassified**	**unclassified**	**UU**	**3**	

None

DELETIONS: (Include Name, Protocol function - PI/CI/AI/TC/Instructor, Effective date of deletion)

Dr. J. Kevin Grayson, Co-Investigator (Amendment 1 – approved, November 8, 2013)

7. PROBLEMS / ADVERSE EVENTS: Identify any problems or adverse events that have affected study progress. Itemize adverse events that have led to unanticipated animal illness, distress, injury, or death; and indicate whether or not these events were reported to the IACUC.

None

8. REDUCTION, REFINEMENT, OR REPLACEMENT OF ANIMAL USE:

REPLACEMENT (ALTERNATIVES): Since the last IACUC approval, have alternatives to animal use become available that could be substituted in this protocol without adversely affecting study or training objectives?

A small animal model using rodents (mice/rats) with a splinted skin wound should be evaluated . In full thickness excision, the mechanical structure of the dermis is completely disrupted, and various forces in the surrounding dermis and the wound site can change (usually decrease) the dimensions of the wound without actually filling the site with new tissue. This phenomenon is called contracture. This type of wound closure can be counteracted by physical splinting of the wound with retaining rings, biopolymer (e.g., collagen) plugs, or other mechanical devices. This rodent model for wound healing with CorMatrix has not been explored and could possibly be comparable to the rabbit model described in this protocol. This should be explored.

REFINEMENT: Since the last IACUC approval, have any study refinements been implemented to reduce the degree of pain or distress experienced by study animals, or have animals of lower phylogenetic status or sentience been identified as potential study/training models in this protocol?

A thin layer of EMLA cream (2.5% Lidocaine/2.5% Prilocaine) can be applied topically with a sterile cotton tip applicator to ear wounds post operatively to help alleviate pain.

REDUCTION: Since the last IACUC approval, have any methods been identified to reduce the number of live animals used in this protocol?

No

9. PUBLICATIONS / PRESENTATIONS: (List any scientific publications and/or presentations that have resulted from this protocol. Include pending/scheduled publications or presentations).

None at this time

10. Were the protocol objectives met, and how will the outcome or training benefit the DoD/USAF?

No, the original objectives of this protocol (pilot study) were to compare healing over time, scar formation and establish a library of histopathology slides for wounds with and without CorMatrix®. Unfortunately, technique perfecting was more challenging than anticipated and the protocol was amended (with IACUC approval) to use 5 animals for technique perfecting instead of only 1. While this increase in animal number did not exceed the original number of 10 animals approved for this protocol, it did not leave enough remaining animals available to conduct the actual pilot study. A new protocol will be submitted to continue the work.

Valuable information was gained from the technique perfecting work that will help investigators move forward with this wound healing model.

11. PROTOCOL OUTCOME SUMMARY: (Please provide, in "ABSTRACT" format, a summary of the protocol objectives, materials and methods, results - include tables/figures, and conclusions/applications.)

Objective: Technique perfecting for wound healing model in the rabbit

Results: Using the five rabbits for technique perfecting proved very beneficial for the investigator. Multiple lessons were learned.

1. The CorMatrix covered the ear wounds best when they were made slightly larger than the wound. Originally, the ear wounds and CorMatrix patches were both cut with a 6mm biopsy punch. This made stitching the patch in place on all sides difficult. The patch was flush with the wound on one side and not necessarily on the opposite side. When the wound was made with a 5mm biopsy punch and the patch with the 6mm punch, the patch easily covered the entire wound on all sides when secured in place.

2. Four wounds per ear was optimum. More than four wound made it difficult (if not impossible) to avoid lacerating a large blood vessel or creating a wound proximal to the ear orifice (an area difficult to place a wound dressing). It also made it difficult to maintain consistent spacing between each wound in an area of the ear that could have a dressing applied.

3. The original spacing between the wounds was 30 mm. That is much larger than necessary or desired. The 30mm distance made applying a dressing to cover all four wounds challenging. Making the wounds 10-15mm apart kept the wounds far enough apart to easily suture the treatment patches in place and not cross contaminate the controls. It also made it much easily to apply a dressing to the ears.

4. Each stitch required a minimum of four throws to tack the CorMatrix in place on four quadrants. The PDS suture has memory and easily unties when not adequately secured. In the first animals, only two throws per stitch were performed and the patches did not remain in place. Upon examination of corresponding histology slides there was no evidence of the CorMatrix patches. When four throws were used to secure the patches, the patch was verified by the histology results.

5. The 5-0 PDS worked much better than 5-0 Vicryl for suturing the patches in place. The Vicryl did not move through the tissue and cartilage smoothly (it was very rough).

6. The Tegaderm dressing worked best when only a small piece was (cut to size) used on the ear. However it would only last one day at best, before coming off the ear. Bacitracin ointment applied twice a day worked well to keep the wound beds moist. However, the bacitracin ointment applied to the wounds with a Vaseline/petroleum gauge place over it appeared to be the best ear dressing (for maintain wound moisture) and would remain in place for at least a day (possibly two days) before changing.

7. EMLA cream could also be applied post operatively before the dressing is applied for postoperative analgesia.

8. The wounds healed very quickly and were completely healed before 28 days post wounding.

(PI / TC Signature)

15 May 2014
(Date)